have shown neutrophil migratory accuracy to be reduced in COPD. This is thought to contribute to the destruction of lung parenchyma and the poor responses seen in infective exacerbations. We aimed to characterise neutrophil migration in COPD and assess whether physiologically relevant concentrations of simvastatin altered neutrophil migration.

Methods Neutrophils were isolated from COPD patients and healthy smoking age-matched controls (age > 60yrs, n = 13 per group) and incubated with 1nM - 1uM Simvastatin or with a control carrier before migratory dynamics were assessed towards IL8 and fMLP using time-lapse photography. Data is expressed as means with standard deviation in parentheses.

Results COPD neutrophils displayed reduced chemotaxis (directional speed of migration) and reduced chemotactic accuracy (Chemotactic Index - a vector analysis of migratory tracks) compared to cells from healthy age-matched controls (HC) in the presence of IL8 and fMLP, replicating previous work. For example, Chemotactic Index: IL8; HC, 0.42CU (0.03), COPD 0.22CU (0.05), p = 0.002; fMLP; HC, 0.34CU (0.05), COPD 0.18CU (0.03) p = 0.014.

Treatment with Simvastatin significantly improved the chemotactic ability of COPD neutrophils in a dose response with greatest improvement seen at the highest concentration (e.g. Chemotaxis to IL8, Carrier control 0.8um/min (0.2), 1nM Simvastatin 1.3um/min (0.2), p = 0.04; 1uM Simvastatin 1.4um/min (0.2), p = 0.004). A similar improvement was seen in Chemotactic Accuracy (e.g. Chemotactic Index to fMLP, Carrier control 0.17CU (0.03), 1nM Simvastatin 0.26CU (0.02), p = 0.018; 1uM Simvastatin 0.31CU (0.03), p = 0.002).

Conclusions Migratory accuracy of circulating neutrophils is reduced in COPD patients compared with healthy, smoking, age-matched controls but can be restored by treatment with therapeutic concentrations of Simvastatin in vitro. Our data suggest statin therapy might be an adjuvant intervention in COPD, modulating neutrophil responses.

Abstract S114 Figure1 Simvastatin improves neutrophil migration in COPD. Legend. Isolated neutrophils from COPD patients (n = 13) migrated towards IL8 (100nM) or fMLP (100nM) following incubation with carrier control or Simvastatin (1nM or 1uM). Measurements were taken from 10 randomly selected cells from each individual. The average results for each subject were calculated, and an overall average was used for comparisons across groups using analysis of variance. Bars represent the mean migratory parameter with standard deviation shown as the error line. * = significant difference in migratory parameter from carrier control data across groups (p < 0.05).

Physiological measurement of breathlessness and breathing

Introduction Breathlessness is the main cause of suffering in COPD. Its brain mechanisms remain poorly understood, yet may represent a novel therapeutic avenue. Until now, functional magnetic resonance imaging (fMRI) studies of breathlessness have been limited to experiments in healthy volunteers. fMRI demonstrates that imagination of painful events engages the same brain networks responsible for perception of physical pain. We